REMARKS

I. Status of the Application

Claims 48-147 and 166-207 are presently pending in the application. Applicants hereby affirm the election of group 1 claims 48-147 and 166-207 for prosecution on the merits. Claims 48-147 and 166-207 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Cozzette *et al.* (U.S. Patent No. 5,200,051) alone, and over Cozzette *et al.* in view of Sanz (U.S. Patent No. 3,615,240).

Applicants have amended the claims under consideration to more clearly define and distinctly characterize Applicants' novel invention. Specifically, Applicants have amended claims 48, 82, 117, 146 and 147 to recite a droplet of less than 5 nl, support for which can be found at page 28, lines 12-14 of the specification, i.e. "droplets of five nanoliters or smaller". The amendments contain no new matter. Attached hereto is a marked-up version of the changes made to the claims captioned "Version of Amendments With Markings To Show Changes Made."

II. Claims 48-147 and 166-207 are Patentable over Cozzette et al. Alone or in Combination with Sanz

At page 4, paragraph 5 of the present Office Action, claims 48-147 and 166-207 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cozzette *et al.* The Examiner states it would have been obvious to (1) make an array with 100-1,000,000 sites in order to mass manufacture 100-1,000,000 sensors at a time; (2) make the droplets cover small areas in order to cover microfabricated electrical elements as disclosed; (3) provide reference points for the visual

recognition system as was known in the art; (4) use known dispensing methods for their known dispensing functions; and (5) use known methods of object location for their known location/placement functions.

At pages 5 and 6 of the instant Office Action, the Examiner states that Cozzette fails to teach dispensing less than 5 nl, the specific size of the array, or coverage of the droplets. The Examiner has modified the disclosure of Cozzette et al. with the disclosure of Sanz which the Examiner states teaches dispensing volumes on the order of 1 nl. The Examiner states that one would modify Cozzette et al. with Sanz in order to use minimal reagents as taught by Cozzette et al.

Applicants respectively traverse the rejections as to the amended claims now presented. Amended claims 48, 117, 146 and 147 and claims depending therefrom are directed to methods of forming arrays of compounds comprising dispensing a droplet of less than 5 nl from a dispenser. Claim 166 is directed to dispensing a plurality of polymers from an array of dispensing units to form the claimed array of polymers.

Cozzette et al. does not teach dispensing a droplet of less than 5 nl as stated by the Examiner. Furthermore, Cozzette does not suggest that it may be modified to dispense less than 5 nl droplets. Cozzette et al. states that drops between about 5 to 500 nl can be dispensed. However, Cozzette et al. dispenses volumes sufficient to cover electrodes. Cozzette et al.'s working examples indicate that at least 10 nl is used in order to effectively cover the indicator electrode of the microfabricated sensor. Cozzette et al. provide no teaching that amounts on the order of 5nl would be sufficient to achieve this application. The Examiner's attention is respectfully directed to col. 72 lines 16-19, col. 72 line 67 to col. 73 line 2 and col. 73 lines 52-

55, where Cozzette et al. teaches depositing "sufficient material" (10 – 100 nl) equaling three times the diameter of the electrode. ("Sufficient material (10-100 nl) is deposited in this technique to allow for the coverage of an area about three times the diameter of the catalytic iridium electrode.") Similarly, at col. 74 lines 13-16 and 47-49, Cozzette et al. teaches that "sufficient material" (10 – 100 nl), equals two times the diameter of the electrode. ("Sufficient material (10-100nl) is deposited by this technique to allow for the coverage of an area about twice the diameter of the catalytic iridium electrode.") Finally, in column 75, lines 37-41, Cozzette et al. teaches dispensing 10 – 100 nl to overlap an electrode on all sides by at least 30 μm. Clearly, the teachings of Cozzette are directed to completely covering the indicator electrodes present on their sensors. Cozzette et al. provides no teaching that amounts less than 10 nl would provide this important aspect of Cozzette et al.'s invention. In fact, one would not be led to use volumes less than 10 nl because to do so would risk not completely covering the electrode.

Sanz, while disclosing a micropipette capable of dispensing volumes on the order of one nl, would not lead one of skill in the art to modify Cozzette et al. to dispense less than 10 nl in the practice of Cozzette et al.'s invention. Again, Cozzette et al. teaches in its working examples that amounts of 10 nl at a minimum be dispensed to completely cover the electrodes. One would not be motivated to dispense 1 nl volumes as disclosed by Sanz (i.e., 10% of the minimum working example volume employed), since to do so would likely lead to partial electrode covering which is adverse to Cozzette et al.'s invention. The Examiner's stated motivation for combining Sanz with Cozzette et al., i.e. to use minimal reagents as taught by Cozzette,

respectfully misses the mark on what Cozzette et al. motivates, if anything. Cozzette et al. teaches the dispensing of volumes sufficient to completely cover the electrodes. In fact, Cozzette et al. teaches that the volume of reagent in one embodiment be such that it covers up to three times the diameter of the electrode. Cozzette et al., therefore, does not motivate one to dispense smaller and smaller volumes of fluid so as to use minimal reagents, as suggested by the Examiner, since Cozzette et al. advises that more reagent be dispensed than can be detected by the sensor. Cozzette et al. encourages overuse of reagent dispensed at the sensors, and does not encourage minimal reagent use.

Furthermore, one of skill in the art would not look to the pipette of Sanz to modify the apparatus of Cozzette et al. Cozzette et al. teaches an automated microfabricating process which comprises a syringe which distributes liquid under the control of pulses of a pressurized gas regulated by a solenoid valve (column 58, lines 44-54, column 59, lines 18-26). In contrast, Sanz describes a manual pipette which has a tubular handle, (1), and distributes liquid by the rotational movement of a ring, (4) (column 2, lines 3-14, Figure 15). There is nothing in Sanz that would suggest the use of its pipette in an automated system. One would not have a reasonable expectation of success using the manual pipette of Sanz in the automated system of Cozzette et al.

Regarding the Examiner's statement that Cozzette et al. teaches a dispenser comprising an array of dispensing units, Applicants respectfully disagree. Claims 117, 146, 147 and 166 and claims depending therefrom are directed to methods of forming arrays of polymers on a support comprising dispensing polymers from a dispenser having an array of dispensing units, wherein polymers are dispensed from the array of dispensing units to produce an array of at least 100

polymers. Thus, Applicants' invention allows the dispensing of multiple polymers simultaneously. Cozzette et al. teaches a microdispensing system which comprises multiple syringe holders (column 17, lines 28-33). Figure 13 of Cozzette et al. illustrates four separate syringe holders. Cozzette et al. does not teach a single dispensing unit containing an array of dispensers, but instead teaches multiple (i.e., four) separate dispensing units. Furthermore, since the syringe itself is bulky relative to the wafer (see Figure 12 , and compare the syringe (5) to the wafer (2)) and the syringe is placed into a single opening (13) of an even bulkier syringe holder (Figure 13), the apparatus taught by Cozzette et al. would not be amenable to depositing more than one sample at a time, and certainly would not be amenable to depositing an array of samples at the same time. Therefore, Cozzette et al. fails to teach or suggest a dispenser having an array of dispensing units, wherein polymers are dispensed from the array of dispensing units to produce an array of at least 100 polymers.

IV. CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at the number below.

Respectfully submitted,

Dated: April 12, 2002

John P. Iwanicki, Reg. No. 34,628
BANNER & WITCOFF, LTD.
28 State Street, 28th Floor
Boston, MA 02109
(617) 227-7111

Version of Amendments with Markings to Show Changes Made

48. (Amended) A method of forming an array of compounds on a support having one or more localized areas comprising

(a) locating a dispenser containing a solution comprising a compound a distance away from a surface of the support;

(b) dispensing a droplet of less than 5 nl [or less] from the dispenser, with the droplet contacting the surface at a localized area smaller than 1 cm^2;

(c) allowing the compound to attach directly or indirectly to the surface of the support at the localized area;

(d) repeating steps a through c to attach a same or different compound at a same or different localized area until an array of at least 10 different reagents at different localized areas is formed.

82. (Amended) The method of claim 48 wherein the dispenser comprises a plurality of dispensing units, wherein the plurality of dispensing units is in fluid communication with a solution comprising a compound and wherein step b comprises dispensing a droplet of less than 5 nl [or less] from one or more of the plurality of dispensing units.

117. (Amended) A method of forming an array of compounds on a support having one or more localized areas comprising

(a) locating a dispenser comprising a plurality of dispensing units a distance away from a surface of the support, wherein the plurality of dispensing units is in fluid communication with a solution comprising a nucleic acid or polypeptide;

(b) dispensing at least one droplet of less than 5 nl [or less] from the dispenser, with the at least one droplet contacting the surface at a localized area smaller than 1 cm^2;

(c) allowing the nucleic acid or polypeptide to attach directly or indirectly to the surface of the support at the localized area;

(d) repeating steps a through c to attach a same or different nucleic acid or polypeptide at a same or different localized area until an array of at least 10 different compounds at different localized areas is formed.

146. (Amended) A method of forming an array of nucleic acids on a support having one or more localized areas comprising

(a) moving a dispenser containing a solution comprising a nucleic acid having greater than 100 monomers toward a surface of the support;

(b) dispensing a droplet of less than 5 nl [or less] from the dispenser, with the droplet contacting the surface at a localized area smaller than 100 μm^2;

(c) allowing the nucleic acid to attach directly or indirectly to the surface of the support at the localized area;

(d) repeating steps a through c to attach a same or different nucleic acid at a same or different localized area until an array of at least 1000 different reagents at different localized areas is formed.

147. (Amended) A method of forming an array of nucleic acids on a support having one or more localized areas comprising

(a) moving a dispenser comprising a plurality of pipettes in fluid communication with a solution comprising a nucleic acid having greater than 100 monomers toward a surface of the support;

(b) dispensing at least one droplet of less than 5 nl [or less] from the dispenser, with the at least one droplet contacting the surface at a localized area smaller than 100 μm^2;

(c) allowing the nucleic acid to attach directly or indirectly to the surface of the support at the localized area;

(d) repeating steps a through c to attach a same or different nucleic acid at a same or different localized area until an array of at least 1000 different reagents at different localized areas is formed.

166. (Amended) A method of forming an array of polymers on a support having localized areas comprising

(a) locating a dispenser comprising an array of dispensing units a distance away from a surface of the support; and

(b) dispensing polymers from the array of dispensing units and attaching them onto the surface at the localized areas to produce an array of at least 100 polymers.

167. (Amended) The method of claim 166 wherein the polymers are dispensed as droplets of less than 5 nl [or less].